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Phylloid Hypermelanosis in a Child with Psychomotor Delay, Cicatricial Alopecia, Hearing Loss and Polythelia

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Phylloid hypermelanosis is a rare form of pigmentary mosaicism that has been reported only a few times in the literature (1–6). While phylloid hypomelanosis is linked to trisomy 13, the cause of phylloid hypermelanosis is more obscure (5, 7–13). We describe here a case of phylloid hypermelanosis associated with mild developmental delay, cicatricial alopecia, hearing loss and polythelia.

CASE REPORT

The boy was the first child of healthy unrelated Iraqi parents. He was born at term after an uneventful pregnancy apart from transient elevated liver parameters in his mother. He was small for gestational age, with a birth weight of 2,500 g and birth length of 48 cm. Immediately after birth patchy and striped hyperpigmentations were noted on his skin. He had hypotonia and showed delayed developmental milestones. His language skills were also delayed, e.g. he could only babble at the age of 3 years. Brain magnetic resonance imaging (MRI) was normal, while an automatic auditory brainstem response (AABR) showed a mild conductive slightly asymmetrical hearing impairment with an auditory threshold of 40 dB and 35 dB on the right and left sides, respectively. Dermatological examination revealed widespread leaf-like, oblong and pear-shaped hyperpigmented patches on his trunk (Fig. 1a) and broad hyperpigmented linear lesions on his limbs. No midline separation was noted on the trunk. A swirl of pigmented vellus hairs was seen centrally on his back between his shoulder blades. Slightly asymmetrical facial features were noted, with right-sided hypoplasia of his facial skeleton and an extra tooth on the left side

of his upper jaw (+02). He had a low frontal hairline and darkly pigmented and dense hair, apart from whorled cicatricial alopecia centrally on his scalp (Fig. 2). Skin biopsies from the scalp showed pseudopelade of Brocq. He had polythelia, with 3 nipples on his right side and 2 nipples on his left side (Fig. 1b).

A skin biopsy was taken from a hyperpigmented area on his back, and chromosomal analysis of 12 metaphases of cultured skin fibroblasts showed a normal male karyotype, as did investigation of blood lymphocytes. Two new skin biopsies were subsequently taken from abnormal hyperpigmented skin and normal pigmented skin on his thigh. This time fibroblasts, as well as keratinocytes, were cultured and showed a normal male karyotype 46,XY. Fluorescence *in situ* hybridization (FISH)-investigation with a 13q14 probe (13q14 Vysis) in 200 metaphases of fibroblasts cultured from normal as well as affected skin showed two signals in all investigated cells, making mosaicism of trisomy 13 very unlikely. Oligo-Array-comparative genomic hybridization (CGH) (OGT Syndrome Plus 2×105K) of cultured fibroblasts as well as cultured keratinocytes was performed twice; once with a Promega female control, and once with normal skin as control for affected skin. The results were normal. Culturing of melanocytes was unsuccessful.

DISCUSSION

Pigmentary mosaicism is a descriptive term for skin pigmentation in various patterns representing two or more different clones of cells. The skin changes may be hypo- or hyper-pigmented and the cutaneous patterns can follow the lines of Blaschko, be seen in a chequerboard pattern, a patchy pattern without midline separation or arranged in a phylloid (leaf-like) pattern (14). The type 1 mosaic pattern, following the lines of Blaschko, is the most common mosaic pattern, which can be subclassified into type 1a with narrow bands and type 1b with broad bands. The chequerboard or type 2 pattern shows alternating squares of dyschromia with a sharp midline separation. Type 3 shows a phylloid pattern of hypo- or hyperchromic macules with midline separation and type 4 shows a patchy pattern without midline separation (3).

The patient described here had phylloid hyperpigmentation of his skin on the trunk, consistent with a type 3 mosaic pattern. This leaf-like pattern, reminiscent of a floral ornament or Art Nouveau (Jugendstil) painting, seems to be the rarest mosaic pattern reported in the skin. This pattern is composed of various elements, such as round or oval lesions,



Fig. 1. Clinical features in a 3-year-old boy with (a) phylloid hyperpigmentation on the trunk and (b) polythelia. The circle marks the biopsy site.

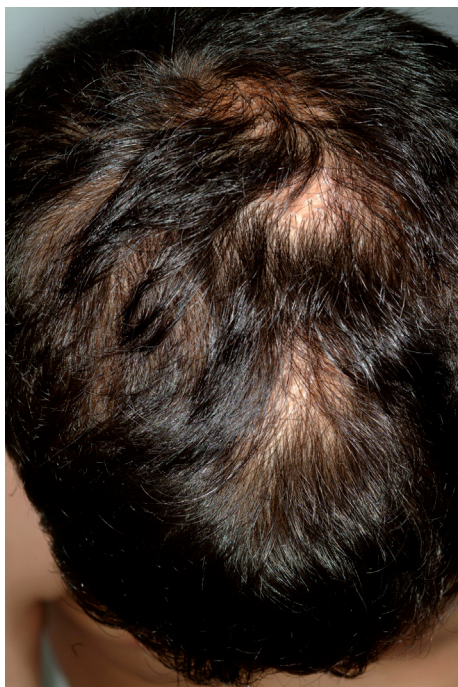


Fig. 2. Whorled cicatricial alopecia centrally on the scalp.

large asymmetrical areas resembling the leaves of a begonia, as well as pear-shaped or oblong macules.

Phylloid hypomelanosis represents a rather uniform neurocutaneous phenotype with associated central nervous system (CNS) defects, conductive hearing loss, choroidal and retinal coloboma, craniofacial and skeletal defects, and appears to be closely linked to abnormalities of chromosome 13, most frequent trisomy 13 (7–13). Phylloid hypermelanosis on the other hand is more rarely seen, and the cause has been revealed in only a few cases. Mosaicism of trisomy 13 has been seen in a patient with a phylloid pattern of hypomelanotic macules as well as slightly hyperpigmented macules (5). Another patient had trisomy based on a translocation $t(13;13)$, with phylloid hypomelanosis and hyperpigmented changes (15). From a clinical point of view these cases may be classified as phylloid hypomelanosis. A patient with phylloid hypermelanosis and melanocytic naevi had ring chromosome 13, with some cells having lost or doubled the ring chromosome (6), a typical mosaic pattern for ring chromosomes in general. Mosaicism of 5p trisomy was seen in a patient with suspected phylloid hypermelanosis from our department (1); however, she was later re-classified clinically as a type 2 mosaic pattern (chequerboard). Two patients did not have cytogenetic investigations performed (2, 4). Based on these data it is still unclear whether phylloid hypermelanosis is a rather uniform neurocutaneous phenotype or is more clinically and genetically diverse than its hypomelanotic counterpart (16). We have searched for, but not found, any cytogenetic abnormality in our patient. We have thus excluded small quantitative chromosomal changes throughout the genome changes (microdeletions and

microduplications of a size of approximately >50 kb) in blood, fibroblasts, and keratinocytes, and with high certainty excluded mosaicism of full trisomy 13. The cause of the phylloid hypermelanosis and associated abnormalities in our patient is thus still unknown, but is most likely monogenic, caused by mosaicism of a point mutation or a small deletion or duplication. An imprinting defect or a low-grade mosaicism of a chromosomal defect other than trisomy 13 cannot be excluded.

The authors declare no conflicts of interest.

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